REMARKS

The Applicant expresses appreciation to the Examiner for consideration of the subject patent application. Applicants further express appreciation for the interview granted the undersigned and Mr. David Osborne by Examiners Count and Le on July 7, 2004.

During the course of the interview the undersigned indicated that the invention was primarily directed to the determination and quantification of phosphoinositide kinase activity. It was pointed out that the prior art, Kingsmore et al. and Czech et al., did not teach methods for the determination of phosphoinositide kinase (or any other enzymatic) activity. It was pointed out by the Examiners that the claims were not so limited and that, if they were, where would be a reconsideration of the prior art in view of such limitations.

Therefore, this amendment is in response to the Office Action mailed April 19, 2004 and the interview conducted on July 7, 2004. New claims 49 to 67 have been added and all previous claims have been canceled. In view of this all previous rejections are believed to be moot. However, it is to be noted that the newly submitted claims are all directed to the same subject matter as was contained in Group II(claims 17-34), which were the elected claims of a restriction requirement issued on December 17, 2003. This is believed to be in conformity with the telephone interview held with the Examiner on March 31, 2004 wherein Applicant confirmed the provisional election of Group II (Claims 17-34) with the proviso that, based on the arguments filed in Applicant's response on January 20, 2004, Claims 1-13 and 16 were regrouped with Group II. Based on an election requirement the elected invention comprised claims 1-13, 16-30, 33 and 34. As stated above, newly submitted claims 49 to 67 are believed to fall within the scope of the Group II elected claims. Certain claim language which was objected to under 35 USC 112 which is believed to have been corrected in the newly submitted claims. The support for the newly submitted claims can be found throughout the specification and no new matter had been introduced.

A new oath or declaration in compliance with 37 CFR 1.67(a) is also enclosed.

Previous Claim Rejections - 35 U.S.C. § 103

Canceled claims 1-7, 9-13, 16-30, 33-34 (including independent claim 1) were rejected under 35 U.S.C. § 103 as being unpatentable over Kingsmore et al. (US 6,531,283)(hereafter referred as "Kingsmore") in view of Czech et al. (US 6,194,173)(hereafter referred as "Czech").

In response to the Examiners' opinion that the claims previously submitted were not limited to a method of determining and quantifying kinase enzyme activity, a new set of claims has been submitted which are specifically drawn to this method, and to a kit for use in making such determinations and quantifications.

In order to most succinctly explain why the claims presented herein are allowable, the Applicant will direct the following remarks primarily to independent claim 49 with the understanding that once an independent claim is allowable, all claims depending therefrom are allowable.

The applicant respectfully submits that the presently submitted claims are not obvious in view of the reference cited. In other words, one of ordinary skill in the art, when combining all teachings of the reference of record at the time of the invention was made, would not have been motivated to come up with the presently claimed invention.

The initial burden is on the Examiner to establish a case of *prima facie* obviousness. The test for establishing such a case is well stated in *In re Vaeck*, 947 F.2d 488, 20USPQ2d 1438 (Fed. Cir.1991) as follows:

> "To establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and reasonable expectation of success must both be found in the prior art, and not based on the applicant's disclosure."

When applying 35 U.S.C. 103, the following tenets of patent law must be adhered to: (A) The claimed invention must be considered as a whole; (B) The references must be considered as a whole and must suggest the desirability and thus the obviousness of making the combination; (c) The references must be viewed without the benefit of impermissible hindsight vision afforded by the claimed invention; and (D) reasonable expectation of success is the standard with which obviousness is determined. Hodosh v. Block Drug Co., Inc., 786 F.2d 1136, 1143 n.5, 229 USPQ 182,187 n.5 (Fed. Cir. 1986)

Under this statement of law, the Applicants respectfully submit that the present invention would not be obvious over Kingsmore in view of Czech.

Kingsmore discloses compositions and methods for detecting small quantities of analytes such as proteins and peptides. The method involves associating a primer with an anylate and subsequently using the primer to mediate the rolling circle replication of a circular DNA molecule. Amplification of the DNA circle is dependent on the presence of the primer. Thus, the disclosed method produces an amplified signal, via rolling circle amplification, from any analyte of interest. The amplified DNA remains associated with the analyte, via the primer, and so allow for spatial detection of the analyte. In other words, Kingsmore requires associating a primer with an anylate which produces an amplified signal, via rolling circle amplification. Although Kingsmore mentions "lipid" in its broad description of possible analytes, it does not describe what lipid and how that lipid can be assayed. However, the present invention as claimed in the amended claims, is directed to "a method for the quantification of phosphoinositide kinase activity, which comprises: exposing a protein, having a phosphoinositide lipid recognition motif that interacts with (a) a target lipid compsising a phosphorylation product of a reaction between the phosphoinositide kinase and a substrate phosphoinositide lipid and (b) a competing phosphoinositide lipid which is labeled by a non-radioactive signal, to an analyte solution containing a determined amount of said competing labeled phosphoinositide lipid and and inknown amount of said target lipid; and quantifying the target lipid in said analyte solution by measuring variation of said non-radioactive signal, wherein said target lipid has a stronger

affinity for said protein having a phosphoinositide lipid recognition motif than said competing lipid.

Therefore, it is respectfully submitted that the present invention as claimed in the presently submitted independent claims 49 and 60 differ from the prior art in that neither Kingmore et al nor Czech et al are drawn to method for identifying and determining phosphoinositide kinase activity. Moreover Kingmore requires amplification of the signal, while the present invention measures variations of a determined amount of signal; and Kingsmore requires the analyte to be bound to a nucleic acid primer, while analyte of the present invention, a phosphorylation product of a reaction between a phosphoinositide kinase and a substrate phosphoinositide lipide is competing for binding with a lipid binding protein(LRP) which has a lipid recognition motif that is specific to phosphoinositides.

Czech discloses isolated nucleic acid molecules encoding general receptors for phosphoinositide(GRPs) peptides and methods of using thereof. Czech teaches methods of modulating Grp1 activity as a nucleotide exchange factor and modulator of cell adhesion, use of Grp1 as an agent to affect membrane trafficking, screening and assays for agents that affect Grp1 activity or Grp1 interaction with a ligand, and screening and assays for agents that affect Grp1 expression. Nothing in Czech teaches or suggests using Grp1 as a specific detector for a lipid or to determine the activity of a lipid kinase. Therefore, the present invention differs from Czech because the present invention relates to the determination of lipid kinase activity, while Czech relates to a lipid binding protein. Nothing in Czech discloses or teaches a method for determining lipid kinase activity method as claimed in the present invention.

There is no motivation to combine the Kingsmore and Czech references. The references teach away from each other because Kingsmore teaches methods for detecting small quantities of analytes such as proteins and peptides, while Czech teaches cloning and purifying Grp1 proteins. Czech discloses methods of modulating Grp1 activity which is not in any way related to methods for detecting small quantities of analytes as taught by Kingsmore. Therefore, it is respectfully submitted that there is no motivation for one skilled in the art to combine the teachings of Kingsmore and Czech.

In addition, the Kingsmore and Czech references, when combined, still do not teach or suggest the elements of the independent claim 49. Specifically, the Kingsmore reference does

not teach the step of exposing a protein, having a phosphoinositide lipid recognition motif that interacts with (a) a target lipid comprising a phosphorylation product of a reaction between the phosphoinositide kinase and a substrate phosphoinositide lipid and (b) a competing phosphoinositide lipid which is labeled by a non-radioactive signal, to an analyte solution containing a determined amount of said competing labeled phosphoinositide lipid and unknown amount of said target lipid Kingsmore also does not teach or suggest the step of quantifying the target lipid by measuring variation of said non-radioactive signal. In addition, the Czech reference does not overcome these deficiencies because those elements are neither taught nor suggested in Czech.

Therefore, it is respectfully submitted that the Examiner has failed to establish a case of *prima facie* obviousness because: first, there is no suggestion or motivation to modify the reference or to combine reference teachings; second, there is no reasonable expectation of success and finally, the prior art references, even when combined, still fail to teach or suggest all the limitations as claimed in the present invention. Therefore, the Applicant respectfully submits that Claims 49 to 67 are allowable.

CONCLUSION

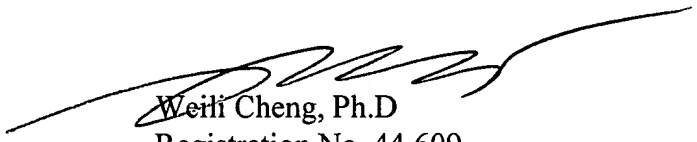
In light of the above, the Applicant respectfully submits that pending claims are now in condition for allowance. Therefore, the Applicant requests that the claims be allowed and passed to issue. If any impediment to the allowance of these claims remains after entry of this Amendment, the Examiner is strongly encouraged to call Weili Cheng Ph.D, or in her absence, the undersigned at (801) 566-6633 so that such matters may be resolved as expeditiously as possible.

Check No. 20525, in the amount of $490.00, is enclosed pursuant to 37 C.F.R. § 1.17(a)(3), for a three month extension of time pursuant to 37 C.F.R. § 1.136. 19 claims were added (claims 49-67), including 2 independent claims (claims 49,60), while 48 claims were canceled (claims 1-48), including independent claims (claims 1,17,35,40). Therefore, no additional fee is due.

The Commissioner is hereby authorized to charge any additional fee or to credit any overpayment in connection with this Amendment to Deposit Account No. 20-0100.

DATED this 18th day of October, 2004.

Respectfully submitted,



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